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NEWS 3	JUL 02	SCISEARCH enhanced with complete author names
NEWS 4	JUL 02	CHEMCATS accession numbers revised
NEWS 5	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 6	JUL 16	CAplus enhanced with French and German abstracts
NEWS 7	JUL 18	CA/CAplus patent coverage enhanced
NEWS 8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9	JUL 30	USGENE now available on STN
NEWS 10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 11	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 12	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 13	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 14	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 15	AUG 27	USPATOLD now available on STN
NEWS 16	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 17	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 18	SEP 13	FORIS renamed to SOFIS
NEWS 19	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 20	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 21	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 22	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 23	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 24	OCT 19	BEILSTEIN updated with new compounds
NEWS 25	NOV 15	Derwent Indian patent publication number format enhanced
NEWS 26	NOV 19	WPIX enhanced with XML display format
NEWS 27	NOV 30	ICSD reloaded with enhancements
NEWS 28	DEC 04	LINPADOCDB now available on STN

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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NEWS IPC8	For general information regarding STN implementation of IPC 8

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FILE 'HOME' ENTERED AT 11:33:18 ON 07 DEC 2007

=> file caplus
COST IN U.S. DOLLARS

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FULL ESTIMATED COST	0.21	0.21

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FILE COVERS 1907 - 7 Dec 2007 VOL 147 ISS 25
FILE LAST UPDATED: 6 Dec 2007 (20071206/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

```
=> s PDE activity
          5611 PDE
          1080 PDES
          6054 PDE
                 (PDE OR PDES)
       2285827 ACTIVITY
        455568 ACTIVITIES
       2477934 ACTIVITY
                 (ACTIVITY OR ACTIVITIES)
L1         914 PDE ACTIVITY
                 (PDE(W)ACTIVITY)

=> s l1 and FP assay?
          9045 FP
          1278 FPS
         10116 FP
                 (FP OR FPS)
        579837 ASSAY?
            75 FP ASSAY?
                 (FP(W)ASSAY?)
L2           0 L1 AND FP ASSAY?

=> s FP assay?
          9045 FP
          1278 FPS
         10116 FP
                 (FP OR FPS)
        579837 ASSAY?
```

```
L3           75 FP ASSAY?
                  (FP(W)ASSAY?)

=> s l3 and inflammatory?
         192527 INFLAMMATORY?
L4            1 L3 AND INFLAMMATORY?

=> d ibib abs hitstr tot
```

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:1090909 CAPLUS
DOCUMENT NUMBER: 147:406707
TITLE: Preparation of quinoline derivatives as PDE4 inhibitors
INVENTOR(S): Edlin, Christopher David; Holman, Stuart
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 38pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007107499	A1	20070927	WO 2007-EP52478	20070315

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2006-5462 A 20060317

OTHER SOURCE(S): MARPAT 147:406707
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. with general formula I [wherein R1 = alkyl or cycloalkyl; R2 = halo or CN] or pharmaceutically acceptable salts or solvates thereof were prepared as inhibitors of phosphodiesterases (PDEs) for the treatment or prophylaxis of diseases for which a PDE4 inhibitor is indicated, in particular, inflammatory or allergic diseases such as chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis, or allergic rhinitis. For example, 4-[(3-chlorophenyl)amino]-8-methyl-6-(4-piperidinylsulfonyl)-3-quinolinecarboxamide dihydrochloride (preparation given) was reacted with iso-Pr sulfonyl chloride in presence of N,N-diisopropylethylamine in N,N-dimethylformamide to give II as a final product. I showed PDE4 inhibitory activity with IC50 values of >9.5 in fluorescence polarization (FP) assays.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s l3 and allerg?
         75412 ALLERG?
L5           1 L3 AND ALLERG?

=> d ibib abs hitstr tot
```

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:1090909 CAPLUS
DOCUMENT NUMBER: 147:406707
TITLE: Preparation of quinoline derivatives as PDE4 inhibitors
INVENTOR(S): Edlin, Christopher David; Holman, Stuart
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 38pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007107499	A1	20070927	WO 2007-EP52478	20070315

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2006-5462 A 20060317

OTHER SOURCE(S): MARPAT 147:406707
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. with general formula I [wherein R1 = alkyl or cycloalkyl; R2 = halo or CN] or pharmaceutically acceptable salts or solvates thereof were prepared as inhibitors of phosphodiesterases (PDEs) for the treatment or prophylaxis of diseases for which a PDE4 inhibitor is indicated, in particular, inflammatory or allergic diseases such as chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis, or allergic rhinitis. For example, 4-[(3-chlorophenyl)amino]-8-methyl-6-(4-piperidinylsulfonyl)-3-quinolinecarboxamide dihydrochloride (preparation given) was reacted with iso-Pr sulfonyl chloride in presence of N,N-diisopropylethylamine in N,N-dimethylformamide to give II as a final product. I showed PDE4 inhibitory activity with IC50 values of >9.5 in fluorescence polarization (FP) assays.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s l1 and inflammatory?
        192527 INFLAMMATORY?
L6          40 L1 AND INFLAMMATORY?

=> s l6 and allerg?
         75412 ALLERG?
L7           9 L6 AND ALLERG?

=> d ibib abs hitstr tot
```

L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1105075 CAPLUS
DOCUMENT NUMBER: 146:19897
TITLE: Inhibition of phosphodiesterase activity, airway inflammation and hyperresponsiveness by PDE4 inhibitor
and glucocorticoid in a murine model of allergic asthma
AUTHOR(S): Sun, Jian-gang; Deng, Yang-mei; Wu, Ximei; Tang, Hui-fang; Deng, Jun-fang; Chen, Ji-qiang; Yang, Shui-you; Xie, Qiang-min
CORPORATE SOURCE: Zhejiang Respiratory Drugs Research Laboratory of State Food and Drug Administration, Medical Science College of Zhejiang University, Hangzhou, 310031, Peop. Rep. China
SOURCE: Life Sciences (2006), 79(22), 2077-2085
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Phosphodiesterase 4 (PDE4) isoenzyme plays important roles in inflammatory and immunomodulatory cells. In this study, piclamilast, a selective PDE4 inhibitor, was used to investigate the role of PDE4 in respiratory function and inflammation in a murine asthma model.
Sensitized mice were challenged with aerosolized ovalbumin for 7 days, piclamilast (1, 3 and 10 mg/kg) and dexamethasone (2 mg/kg) were orally administered once daily during the period of challenge. Twenty-four hours
after the last challenge, airway hyperresponsiveness to methacholine was determined by whole-body plethysmog., airway inflammation and mucus secretion
by histomorphometry, pulmonary cAMP-PDE activity by HPLC, cytokine levels in bronchoalveolar lavage fluid and their mRNA expression in lung by ELISA and RT-PCR, resp. In control mice, significant induction of cAMP-PDE activity was parallel to the increases of hyperresponsiveness, inflammatory cells, cytokine levels, mRNA expression as well as goblet cell hyperplasia. However, piclamilast dose-dependently and significantly improved airway resistance and dynamic compliance, and the maximal effect was similar to that of dexamethasone. Piclamilast treatment dose-dependently and significantly prevented the increase in inflammatory cell number and goblet cell hyperplasia, as well as production of cytokines, including eotaxin, TNFα and IL-4. Piclamilast exerted a weaker inhibitory effect than dexamethasone on eosinophils and neutrophils, had no effect on lymphocyte accumulation. Moreover, piclamilast inhibited up-regulation of cAMP-PDE activity and cytokine mRNA expression; the maximal inhibition of cAMP-PDE was greater than that exerted by dexamethasone, and was similar to dexamethasone on cytokine mRNA expression. This study suggests that inhibition of PDE4 by piclamilast robustly improves the pulmonary function, airway inflammation and goblet cell hyperplasia in murine allergenic asthma.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:967566 CAPLUS
DOCUMENT NUMBER: 145:369507
TITLE: Effects of ciclamilast, a new PDE4 inhibitor, on airway hyperresponsiveness, PDE4D expression and airway inflammation in a murine model of asthma
AUTHOR(S): Deng, Yang-mei; Xie, Qiang-min; Tang, Hui-fang; Sun, Jian-gang; Deng, Jun-fang; Chen, Ji-qiang; Yang, Shui-you
CORPORATE SOURCE: Zhejiang Respiratory Drugs Research Laboratory Of State Food And Drug Administration, Medical Science College Of Zhejiang University, Hangzhou, Peop. Rep. China
SOURCE: European Journal of Pharmacology (2006), 547(1-3), 125-135
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB PDE4 (phosphodiesterase-4) plays a critical role in pathogenesis of allergic asthma and chronic obstructive pulmonary disease (COPD). PDE4 inhibitors are presently under clin. development for the treatment of
asthma and/or COPD. Ciclamilast, a new PDE4 inhibitor, is a piclamilast (RP 73401) structural analog, but has a more potent inhibitory effect on PDE4 and inflammation in the airway tissues and less side effects than that of piclamilast. In this study, we elucidate primarily on the roles of compound on PDE4 enzyme in physiol. and pathol. processes in a mouse model of asthma. The sensitized/challenged mice were reexposed to ovalbumin and airway response to inhaled methacholine was monitored. Orally administration of ciclamilast, in a dose-dependent manner, significantly inhibited changes in lung resistance and lung dynamic compliance, as well as upregulation of cAMP-PDE activity , increase of PDE4D mRNA expression, but not PDE4B from lung tissue in the
murine model. In addition, the compound dose-dependently reduced mRNA expression of eotaxin, tumor necrosis factor (TNF)-α and interleukin (IL)-4, but slightly increased mRNA expression of interferon (IFN)-γ from lung tissue. Further, levels of eotaxin, TNF-α and IL-4, and eosinophil and neutrophil accumulation in bronchoalveolar lavage fluid were also significantly reduced. Pathol. examination, goblet cell hyperplasia
and inflammatory cells infiltration in lung tissue were suppressed by treatment with ciclamilast. A significant correlation was observed between the increases in PDE4D mRNA expression and airway hyperresponsiveness. These studies confirm that inhibitory effect of ciclamilast on airway hyperresponsiveness includes its inhibiting PDE4D mRNA expression, down-modulating PDE4 activity, anti-inflammation and anti-mucus hypersecretion, and ciclamilast may have therapeutic potential for the treatment of asthma.
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

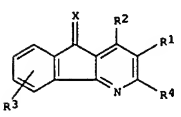
L7 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:521711 CAPLUS
DOCUMENT NUMBER: 144:487025
TITLE: The role of PDE4 in pulmonary inflammation and goblet cell hyperplasia in allergic rats
AUTHOR(S): Tang, Hui-Fang; Chen, Ji-Qiang; Xie, Qiang-Min; Zheng,
Xu-Yang; Zhu, Yi-Liang; Adcock, Ian; Wang, Xiangdong
CORPORATE SOURCE: Zhejiang Respiratory Drugs Research Laboratory of State Foods and Drugs Administration of China, Medical
School of Zhejiang University, Hangzhou, 310031, Peop.
Rep. China
SOURCE: Biochimica et Biophysica Acta, Molecular Basis of Disease (2006), 1762(5), 525-532
CODEN: BBADEX; ISSN: 0925-4439
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Phosphodiesterase 4 (PDE4) has been suggested to a critical factor in the pathogenesis of inflammation by metabolizing cAMP in human leukocytes, endothelium and epithelium. The present study aimed at evaluating the PDE4 activity and expression, the relation between the inflammation and cAMP-activity in the lungs, and potential interventions of PDE inhibitors and antiinflammatory drugs in the reduction of lung inflammation and goblet
cell hyperplasia in allergic rats. The total leukocyte number and eosinophil number in bronchoalveolar lavage fluid and PDE4 activity and expression in lungs significantly increased in OVA-sensitized and challenged allergic rat. Lung histol. showed an increased infiltration of inflammatory cells in the perivascular and peribronchial spaces, structure changes and goblet cell hyperplasia in the
OVA-sensitized and -challenged allergic rats. A significant correlation was observed between the increases in cAMP-PDE activity and inflammation in the lung. Those OVA-induced changes were prevented by pretreatment with PDE inhibitor in a dose-related patterns and with glucocorticosteroid. The authors found an increase in the proportion of PDE4 and PDE4 gene expression, while a decrease in the proportion of PDE3 in the lung of allergic rats. Incubation with different PDE inhibitors down-regulated OVA-induced cAMP hydrolysis. The data suggest that PDE4C may play an important role in the airway inflammation, remodeling and goblet cell hyperplasia after repeated challenge of sensitized rats.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:353146 CAPLUS
DOCUMENT NUMBER: 140:375085
TITLE: Preparation of arylindenopyridines as phosphodiesterase inhibitors and adenosine A2a receptor antagonists
INVENTOR(S): Heintzelman, Geoffrey R.; Averill, Kristin M.; Dodd, John H.; Demarest, Keith T.; Tang, Yuting; Jackson, Paul F.
PATENT ASSIGNEE(S): Ortho-Muniel Pharmaceutical, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 136 pp., Cont.-in-part of U.S. Pat. Appl. 2003 212,089.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004082578	A1	20040429	US 2002-259139	20020927
US 6903109	B2	20050607		
US 2003212089	A1	20031113	US 2002-123389	20020416
US 6958328	B2	20051025		
US 2004127510	A1	20040701	US 2003-678562	20031003
US 2006154949	A1	20060713	US 2005-42281	20050124
US 2005239782	A1	20051027	US 2005-148114	20050608
US 2005239812	A1	20051027	US 2005-169549	20050629
US 2005239810	A1	20051027	US 2005-170044	20050629
US 2005267142	A1	20051201	US 2005-169554	20050629
US 2005267138	A1	20051201	US 2005-170484	20050629
US 2005267139	A1	20051201	US 2005-170569	20050629
US 2006009481	A1	20060112	US 2005-196154	20050803
US 2005277637	A1	20051215	US 2005-197612	20050804
US 2007155760	A1	20070705	US 2006-560637	20061116

PRIORITY APPLN. INFO.: US 2001-284465P P 20010418
US 2002-123389 A2 20020416
US 2002-259139 A2 20020927
US 2003-678562 A3 20031003
US 2005-42281 A3 20050124

OTHER SOURCE(S): MARPAT 140:375085
GI



I

AB This invention provides novel arylindenopyridines (shown as I; variables

L7 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
defined below and/or in claims; e.g.
4-(3,5-dimethylphenyl)-2-methyl-5-oxo-
5H-indeno[1,2-b]pyridine-3-carboxylic acid Me ester), and pharmaceutical
compns. comprising same, useful for treating disorders ameliorated by
antagonizing adenosine A2a receptors or by reducing phosphodiesterase (
PDE) activity in appropriate cells. I are potent small
mol. phosphodiesterase inhibitors that have demonstrated potency for
inhibition of PDE7, PDE5, and PDE4; some I are potent small mol. PDE7
inhibitors that have also demonstrated good selectivity against PDE5 and
PDE4; data are provided for about 30 I. I are also antagonists of the
adenosine A2a receptors that have demonstrated potency for the antagonism
of adenosine A2a, A1, and A3 receptors; data are provided for about 45 I.
This invention also provides therapeutic and prophylactic methods using
the instant pharmaceutical compns. Although the methods of prepn. are
not
claimed, 23 example prepns. of intermediates and I are included; mass
spectral data are tabulated for 284 examples of I. In I: R1 = COR5,
COOR6, CN, a lactone or lactam formed with R4, CONR7R8; R2 =
(un)substituted alkyl, aryl, heteroaryl, heterocyclyl, cycloalkyl; R3 =
H,
halo, alkyl, arylalkyl, cycloalkyl, alkoxy, CN, carboalkoxy, CF3,
alkylsulfonyl, NO2, OH, OCF3, carboxylate, aryl, heteroaryl,
heterocyclyl;
NR10R11; NR12COR13; R4 = H, alkyl, benzyl, NR13R14; X = S, O; R5, R6 = H,
alkyl, aryl, arylalkyl; R7, R8 = H, alkyl, cycloalkyl, etc.; R10, R11 =
H,
alkyl, arylalkyl, etc.; R12, R14 = H, alkyl; R13 = H, alkyl, alkoxy, etc.
REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR
THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
appropriate cells, were prepd. Thus, oxidn. of dihydropyridine II
(prepn.
given) afforded 81% III. The IC50 and %inhibition data on PDE 4,5 and
7A,
and Ki on A2a and A1 receptors binding for representative compds. I were
given. Pharmaceutical compns. comprising the compd. I are claimed. This
invention also provides therapeutic and prophylactic methods using the
instant pharmaceutical compns.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR
THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:855799 CAPLUS
DOCUMENT NUMBER: 139:350637
TITLE: Preparation of 5-oxo and 5-thio derivatives of 5H-indeno[1,2-b]pyridine with adenosine A2a receptor binding and phosphodiesterase inhibiting activity for the treatment of neurodegenerative disorders and inflammation related diseases
INVENTOR(S): Heintzelman, Geoffrey R.; Averill, Kristin M.; Dodd, John H.; Demarest, Keith T.; Tang, Yuting; Jackson, Paul F.
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003088963	A1	20031030	WO 2002-US30825		20020927
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2003212089	A1	20031113	US 2002-123389		20020416
US 6958328	B2	20051025			
CA 2488929	A1	20031030	CA 2002-2488929		20020927
AU 2002341875	A1	20031103	AU 2002-341875		20020927
BR 2002015699	A	20050503	BR 2002-15699		20020927
CN 1809349	A	20060726	CN 2002-810472		20020927
MX 2004PA10307	A	20060222	MX 2004-PA10307		20041018
IN 2005KN00303	A	20070928	IN 2005-KN303		20041116
ZA 2005001390	A	20060830	ZA 2005-1390		20050216
PRIORITY APPLN. INFO.:			US 2002-123389	A	20020416
			US 2001-284465P	P	20010418
			WO 2002-US30825	W	20020927

OTHER SOURCE(S): MARPAT 139:350637
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

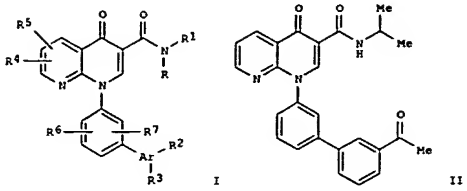
AB The title compds. [I; R1 = COR5 (wherein R5 = H, alkyl, aryl, arylalkyl), CO2R6 (R6 = H, alkyl, aryl, arylalkyl), CN, etc.; R2 = alkyl, aryl, heteroaryl, etc.; R3 = H, halo, alkyl, etc.; R4 = H, alkyl, CH2Ph, etc.; X
= S, O], useful for treating disorders ameliorated by antagonizing adenosine A2a receptors or reducing PDE activity in

L7 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:906219 CAPLUS
DOCUMENT NUMBER: 138:4594
TITLE: Preparation of 1-biaryl-[1,8]naphthyridin-4-one phosphodiesterase IV inhibitors for treatment of asthma and inflammation
INVENTOR(S): Guay, Daniel; Girard, Mario; Hamel, Pierre; Laliberte,
Sebastien; Friesen, Richard; Girard, Yves; Li, Chun
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002094823	A1	20021128	WO 2002-CA746		20020522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2447765	A1	20021128	CA 2002-2447765		20020522
AU 2002257459	A1	20021203	AU 2002-257459		20020522
EP 1397359	A1	20040317	EP 2002-727127		20020522
EP 1397359	B1	20050831			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004534773	T	20041118	JP 2002-591496		20020522
AT 303384	T	20050915	AT 2002-727127		20020522
ES 2247325	T3	20060301	ES 2002-2727127		20020522
US 2003096829	A1	20030522	US 2002-154591		20020524
US 6677351	B2	20040113			
PRIORITY APPLN. INFO.:			US 2001-293247P	P	20010524
			WO 2002-CA746	W	20020522

OTHER SOURCE(S): MARPAT 138:4594
GI

L7 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I II

AB Title compds. I [wherein Ar = Ph, pyridyl, pyrimidyl, indolyl, quinolinyl, thienyl, pyridonyl, oxazolyl, oxadiazolyl, thiadiazolyl, imidazolyl, or heteroaryl oxides; R = H or alkyl; R1 = H or (un)substituted (cyclo)alkyl, alkoxy, alkenyl, alkynyl, heteroaryl, or heterocyclyl; R2 = H, halo, (cyclo)alkyl, alkoxy, amino, acyl, alkoxycarbonyl, alkylsulfamoyl, alkylsulfonyl, or (un)substituted Ph, heteroaryl, or heterocyclyl, etc.; R3 = H, OH, NH2, halo, (un)substituted alkyl; R4-R7 = independently H, halo, NH2, or (un)substituted alkyl or alkoxy; or pharmaceutically acceptable salts thereof] were prepared as phosphodiesterase IV (PDE4) inhibitors for the treatment of asthma and inflammation. For instance, Et 3-(3-bromoanilino)-2-(2-chloronicotinoyl)acrylate was cyclized using NaH in THF and the resulting ester saponified to give 1-(3-bromophenyl)-1,4-dihydro-[1,8]naphthyridin-4-one-3-carboxylic acid. Amidation with isopropylamine, followed by treatment with 3-acetylphenylboronic acid in the presence of trans-PdBr2(PPh3)2 and Na2CO3 in toluene and EtOH gave II.

I demonstrated PDE4 inhibitory activity by suppression of TNF-α secretion in LPS stimulated human blood with IC50 values generally ranging from 0.005 μM to 15.4 μM. In a SPA based PDE activity assay, I inhibited the hydrolysis of cAMP to AMP by human recombinant phosphodiesterase IVa with IC50 values between 34.3 nM and 134.0 nM.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

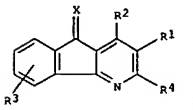
L7 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:832790 CAPLUS
DOCUMENT NUMBER: 137:337793
TITLE: Preparation of arylindenopyridines as phosphodiesterase inhibitors
INVENTOR(S): Heintzelman, Geoffrey R.; Averill, Kristin M.; Dodd, John H.
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085894	A1	20021031	WO 2002-US11823	20020416
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2445188	A1	20021031	CA 2002-2445188	20020416
AU 2002256225	A1	20021105	AU 2002-256225	20020416
EP 1385843	A1	20040204	EP 2002-725675	20020416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1516698	A	20040728	CN 2002-811974	20020416
JP 2004532228	T	20041021	JP 2002-583421	20020416

PRIORITY APPLN. INFO.: US 2001-284465P P 20010418
WO 2002-US11823 W 20020416

OTHER SOURCE(S): MARPAT 137:337793
GI



I

AB This invention provides novel arylindenopyridines (shown as I; variables defined below and/or in claims; e.g. 4-(3,5-dimethylphenyl)-2-methyl-5-oxo-5H-indeno[1,2-b]pyridine-3-carboxylic acid Me ester), and pharmaceutical compns. comprising same, useful for treating disorders ameliorated by reducing phosphodiesterase (PDE) activity in appropriate cells. I are potent small mol. phosphodiesterase inhibitors that have demonstrated potency for inhibition of PDE7, PDE5, and PDE4;

L7 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

some I are potent small mol. PDE7 inhibitors that have also demonstrated good selectivity against PDE5 and PDE4; data are provided for about 30 I. This invention also provides therapeutic and prophylactic methods using the instant pharmaceutical compns. Although the methods of prepn. are not claimed, 21 example prepns. of intermediates and I are included; mass spectral data are tabulated for 263 examples of I. In I: R1 is -COR5, COOR6, cyano, a lactone or lactam formed with R4, -CONR7R8. R2 is optionally substituted alkyl, aryl, heteroaryl, heterocyclyl and C3-7 cycloalkyl. R3 is 1-4 groups H, halo, C1-8 straight or branched chain alkyl, arylalkyl, C3-7 cycloalkyl, C1-8 alkoxy, cyano, C1-4 carboalkoxy, trifluoromethyl, C1-8 alkylsulfonyl, halogen, nitro, hydroxy, trifluoromethoxy, C1-8 carboxylate, aryl, heteroaryl, and heterocyclyl; -NR10R11; -NR12COR13. R4 is H, C1-3 straight or branched chain alkyl, benzyl and -NR13R14. X is S and O.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:50304 CAPLUS
DOCUMENT NUMBER: 137:31970
TITLE: Differential effect of phosphodiesterase inhibitors on IL-13 release from peripheral blood mononuclear cells
AUTHOR(S): Yoshida, N.; Shimizu, Y.; Kitaichi, K.; Hiramatsu, K.; Takeuchi, M.; Ito, Y.; Kume, H.; Yamaki, K.; Suzuki, R.; Shibata, E.; Hasegawa, T.; Takagi, K.
CORPORATE SOURCE: Second Department of Internal Medicine and Laboratory Medicine, Nagoya University School of Medicine, Nagoya, 461-8673, Japan
SOURCE: Clinical and Experimental Immunology (2001), 126(3), 384-389
CODEN: CEXIAL; ISSN: 0009-9104
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Increased cAMP-phosphodiesterase (PDE) activity in peripheral blood leukocytes is associated with the immunol. inflammation that characterizes allergic diseases, such as atopic dermatitis and allergic rhinitis. Recently, it has been found that IL-13 has similar biol. functions to IL-4. The aim here was to investigate the possible involvement of cAMP-PDE activity on IL-13 release from peripheral blood mononuclears cells (PBMC) from atopic asthma patients. Phytohemagglutinin (PHA)-induced IL-13 release from PBMC was concentration-dependently inhibited by rolipram, a type 4 PDE inhibitor, as well as by dibutyryl cAMP, a membrane-permeant cAMP analog. However, theophylline, a non-specific PDE inhibitor, and cilostazol, a type 3 PDE inhibitor, failed to inhibit IL-13 release. The inhibitory effect of rolipram was enhanced by the addition of forskolin (10-4 M), an adenylyl cyclase stimulator. PHA itself did not alter the intracellular cAMP level. Rolipram concentration-dependently increased cAMP level in PHA-stimulated PBMC, and this increase was synergistically facilitated by the addition of forskolin (10-4 M). Thus, type 4 PDE inhibitors, alone or synergistically in combination with forskolin, inhibit PHA-induced IL-13 release from PBMC of atopic asthma patients by elevating intracellular cAMP concns. These inhibitors have the potential to exert an anti-inflammatory effect by inhibiting IL-13 production in allergic diseases such as atopic asthma.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:268097 CAPLUS
DOCUMENT NUMBER: 133:160077
TITLE: Beclomethasone decreases elevations in phosphodiesterase activity in human T lymphocytes
AUTHOR(S): Crocker, I. Caroline; Church, Martin K.; Ohia, S. Edet; Townley, Robert G.
CORPORATE SOURCE: Division of Allergy, Creighton University, Omaha, NE, USA
SOURCE: International Archives of Allergy and Immunology (2000), 121(2), 151-160
CODEN: IAAIEG; ISSN: 1018-2438
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It has been reported that CD4+ T cells that have been activated in vivo or in vitro contain elevated cAMP phosphodiesterase (PDE) activity. Since both PDE inhibitors and glucocorticoids have anti-inflammatory activity, the effect of beclomethasone on PDE activity was investigated. PDE activity was measured in CD4+ T cells after 24 h of culture with beclomethasone. The cells were obtained from the peripheral blood of nonatopic persons (nCells), preseasonal (pCells), seasonal (within the 1st 2 wk; sCells) and midseasonal (mCells) allergic rhinitics and asymptomatic allergic asthmatics (aCells). In addition, the effect of beclomethasone on Th2 cell lines and cells that had been activated in vitro with PHA or interleukin (IL)-2 was determined PDE activity was decreased in a concentration-dependent manner by incubation of mCells, Th2 lines and PHA- or IL-2-activated CD4+ T cells with beclomethasone. However, beclomethasone did not modulate PDE activity in nCells, pCells, sCells, or aCells. Thus, beclomethasone decreases cAMP PDE activity in CD4+ T cells only when it has been increased by cell activation either in vitro or in vivo.
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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     FILE 'CAPLUS' ENTERED AT 11:33:35 ON 07 DEC 2007
L1           914 S PDE ACTIVITY
L2             0 S L1 AND FP ASSAY?
L3            75 S FP ASSAY?
L4             1 S L3 AND INFLAMMATORY?
L5             1 S L3 AND ALLERG?
L6            40 S L1 AND INFLAMMATORY?
L7             9 S L6 AND ALLERG?

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